

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) ~~[[A]]~~The method of claim 52, wherein for inhibiting proliferation of cancer cells comprising:

~~(a) — administering to the cells a first agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1α and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,~~

~~—— the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,~~

~~—— the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,~~

~~—— and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

~~(b) — administering to the cells a second agent comprising~~ the second therapeutic agent is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs~~[[,]]~~

~~wherein the administering steps may be performed simultaneously or sequentially in any order.~~

2. (Original) The method of claim 1, wherein the oligonucleotide is a hybrid oligonucleotide.

3. (Previously Presented) The method of claim 2, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:4.

4. (Currently Amended) The method of claim 1, wherein the second therapeutic agent is an antibody that binds to EGFR.

5. (Original) The method of claim 4, wherein the antibody is a monoclonal antibody.

6. (Original) The method of claim 5, wherein the antibody is C225.

7. (Currently Amended) The method of claim 1, wherein the second therapeutic agent is a taxane.

8. (Original) The method of claim 7, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.

9. (Currently Amended) The method of claim 1, wherein the second therapeutic agent is administered prior to administration of the first therapeutic agent.

10. (Original) The method of claim 1, wherein the cancer cells are human cancer cells.

11. (Original) The method of claim 10, wherein the human cancer cells are selected from the group consisting of breast cancer cells, colon cancer cells, and ovarian cancer cells.

12. (Currently Amended) ~~[[A]]~~The pharmaceutical composition of claim 53, wherein comprising:

~~(a) a first agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide;~~

~~the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides;~~

~~the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides;~~

~~and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

~~(b) a second agent comprising the second therapeutic agent is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs.~~

13. (Previously Presented) The pharmaceutical composition of claim 12, wherein the oligonucleotide is a hybrid oligonucleotide.

14. (Previously Presented) The pharmaceutical composition of claim 13, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:4.

15. (Currently Amended) The pharmaceutical composition of claim 12, wherein the second therapeutic agent is an antibody that binds to EGFR.

16. (Previously Presented) The pharmaceutical composition of claim 15, wherein the antibody is a monoclonal antibody.

17. (Previously Presented) The pharmaceutical composition of claim 12, wherein the antibody is C225.

18. (Currently Amended) The pharmaceutical composition of claim 12, wherein the second therapeutic agent is a taxane.

19. (Previously Presented) The pharmaceutical composition of claim 18, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.

20. (Currently Amended) The pharmaceutical composition of claim 12, wherein the second therapeutic agent is administered prior to administration of the first therapeutic agent.

21. (Cancelled)

22. (Cancelled)

23. (Currently Amended) ~~[[A]]~~ The method of claim 54, wherein for treating cancer in an afflicted subject comprising:

~~(a) administering to the subject a first agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1a and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide;~~

~~—— the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides;~~

~~—— the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides;~~

~~—— and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

~~(b) administering to the subject a second agent comprising the second therapeutic agent is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs[[,]]~~

~~wherein the administering steps may be performed simultaneously or sequentially in any order.~~

24. (Original) The method of claim 23, wherein the oligonucleotide is a hybrid oligonucleotide.

25. (Previously Presented) The method of claim 24, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:4.

26. (Currently Amended) The method of claim 23, wherein the second therapeutic agent is an antibody that binds to EGFR.
27. (Original) The method of claim 26, wherein the antibody is a monoclonal antibody.
28. (Original) The method of claim 27, wherein the antibody is C225.
29. (Currently Amended) The method of claim 23, wherein the second therapeutic agent is a taxane.
30. (Original) The method of claim 29, wherein the taxane is selected from the group consisting of paclitaxel and docetaxel.
31. (Currently Amended) The method of claim 23, wherein the second therapeutic agent is administered prior to administration of the first therapeutic agent.
32. (Previously Presented) The method of claim 23, wherein the subject is a human.
33. (Previously Presented) The method of claim 32, wherein the human has a cancer selected from the group consisting of breast cancer, colon cancer, and ovarian cancer.
34. (Previously Presented) The method of claim 1, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

35. (Previously Presented) The method of claim 34, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

36. (Previously Presented) The method of claim 1, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

37. (Previously Presented) The method of claim 36, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

38. (Previously Presented) The method of claim 1, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

39. (Previously Presented) The pharmaceutical composition of claim 12, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

40. (Previously Presented) The pharmaceutical composition of claim 39, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

41. (Previously Presented) The pharmaceutical composition of claim 12, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

42. (Previously Presented) The pharmaceutical composition of claim 41, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

43. (Previously Presented) The pharmaceutical composition of claim 12, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

44. (Previously Presented) The method of claim 23, wherein the oligonucleotide is an inverted hybrid oligonucleotide.

45. (Previously Presented) The method of claim 44, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:6.

46. (Previously Presented) The method of claim 23, wherein the oligonucleotide is an inverted chimeric oligonucleotide.

47. (Previously Presented) The method of claim 46, wherein the oligonucleotide has a nucleotide sequence consisting of the nucleotide sequence set forth in SEQ ID NO:1.

48. (Previously Presented) The method of claim 23, wherein the oligonucleotide further comprises a 2'-O-substituted nucleotide.

49. (Currently Amended) ~~[[A]]The method of claim 55, wherein for inhibiting proliferation of cancer cells comprising:~~

~~(a) administering to the cells a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1a, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,~~

~~the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,~~

~~the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides;~~

~~and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

(b) ~~administering to the cells a second agent comprising the second~~
therapeutic agent is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs[[,]]

~~wherein the administering steps may be performed simultaneously or sequentially in any order.~~

50. (Currently Amended) [[A]]The pharmaceutical composition of claim 56, wherein comprising:

(a) ~~a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1 α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide;~~

~~the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides;~~

~~the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides;~~

~~— and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

(b) ~~— a second agent comprising the second therapeutic agent~~ is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs.

51. (Currently Amended) ~~[[A]]~~ The method for treating cancer of claim 57, wherein in an afflicted subject comprising:

(a) ~~— administering to the subject a first agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit R1a, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide;~~

~~— the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides;~~

~~— the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides;~~

~~— and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and~~

(b) ~~— administering to the subject a second agent comprising the second~~ therapeutic agent is an antibody that binds to epidermal growth factor receptor (EGFR) or a cytotoxic agent selected from the group consisting of taxanes, platinum-derived agents, and topoisomerase II-selective drugs[[,]]

~~wherein the administering steps may be performed simultaneously or sequentially in any order.~~

52. (New) A method for inhibiting proliferation of cancer cells comprising:

(a) administering to the cells a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the cells a second therapeutic agent comprising an active ingredient for cancer therapy,

wherein the administering steps may be performed simultaneously or sequentially in any order.

53. (New) A pharmaceutical composition comprising:

(a) a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and

wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) a second therapeutic agent comprising an active ingredient for cancer therapy.

54. (New) A method for treating cancer in an afflicted subject comprising:

(a) administering to the subject a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α and having from 0 to 25 additional nucleotides extending from the 3' terminus, the 5' terminus, or both the 3' and the 5' terminus, and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the subject a second therapeutic agent comprising an active ingredient for cancer therapy,

wherein the administering steps may be performed simultaneously or sequentially in any order.

55. (New) A method for inhibiting proliferation of cancer cells comprising:

(a) administering to the cells a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the cells a second therapeutic agent comprising an active ingredient for cancer therapy,

wherein the administering steps may be performed simultaneously or sequentially in any order.

56. (New) A pharmaceutical composition comprising:

(a) a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) a second therapeutic agent comprising an active ingredient for cancer therapy.

57. (New) A method for treating cancer in an afflicted subject comprising:

(a) administering to the subject a first therapeutic agent comprising a synthetic, modified oligonucleotide complementary to at least 15 consecutive nucleotides of the nucleic acid encoding the N-terminal 8-13 codons of protein kinase A subunit RI α , and wherein the oligonucleotide is a hybrid, inverted hybrid, or inverted chimeric oligonucleotide,

the hybrid oligonucleotide comprising a region of at least two deoxyribonucleotides, flanked by 3' and 5' flanking ribonucleotide regions each having at least four ribonucleotides,

the inverted hybrid oligonucleotide comprising a region of at least four ribonucleotides flanked by 3' and 5' flanking deoxyribonucleotide regions of at least two deoxyribonucleotides,

and the inverted chimeric oligonucleotide comprising an oligonucleotide nonionic region of at least four nucleotides flanked by two oligonucleotide phosphorothioate regions; and

(b) administering to the subject a second therapeutic agent comprising an active ingredient for cancer therapy,

wherein the administering steps may be performed simultaneously or sequentially in any order.